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HYPERHAPLOID AND TETRAPLOID SPERM DETECTED IN MEN WHO INGESTED ULTRA-HIGH DOSES OF DIAZEPAM. A. Baumgartner[1,2*], A.E. Czeizel[3*], I.-D. Adler[2*], X. Lowe[1], T.E. Schmid[2*], A.J. Wyrobek[1]. [1]BBRP, Lawrence Livermore Natl. Lab., Livermore, CA; [2]GSF-Inst Säugetiergenetik, Neuherberg, Germany; [3]Dept Hum. Genetics and Teratology, Natl. Inst. Hygiene, Budapest, Hungary.

Diazepam is widely administered as a sedative, muscle relaxant and anxiolytic drug. Five young non-smoking men who were hospitalized after their suicide attempt using diazepam, ~1-7 mg/kg (oral intake), provided semen samples 40-50 days and ~100 days after exposure to assess drug effects on meiotic cells and to evaluate persistence. Five healthy men served as local clinical controls. A multicolor FISH assay was applied to detect aneuploidy for chromosomes X, Y, and 21 in sperm. Sex ratios were not significantly different from 1:1 among 133,143 cells analyzed. The 40-day samples showed an increase in several sperm aneuploidy groups: disomy 21 (1.5 fold, p=0.04); disomy X (2.7 fold, p=0.0006), and XY aneuploidy (1.6 fold, p=0.017). The results for ~100 days after exposure were similar to controls suggesting that hyperhaploidy effects may not persist. Phase contrast microscopy was used to identify flagellated tetraploid sperm, i.e., X-X-Y-Y-21-21-21-21. Tetraploid sperm were found among 8 semen samples provided by five patients (1.4 ± 1.2 per 10,000 cells; >80,000 cells) while none were detected among >50,000 cells from healthy men. Our findings are consistent with the possible aneuploidy-inducing effect of diazepam during male meiosis but further studies are needed before these results can be extrapolated to therapeutic dosing because suicide patients are a highly exposed cohort and other confounding factors (alcohol, drugs, antidotes) cannot be ruled out. [Work was performed under the auspices of the US DOE by the Lawrence Livermore Natl. Lab. under contract W-7405-ENG-48; A.B. was supported by EU contract EV5V-CT94-0403 and the US DOE]